Massachusetts Department of Public Health

State Laboratory Institute

A Monthly Newsletter of the Bureau of Laboratory Sciences

Volume 1, Number 4 April, 1999

Bioterrorism Initiative to Build Public Health Infrastructure

The Centers for Disease Control and Prevention (CDC) released a cooperative agreement announcement to public health agencies on February 27 to upgrade state and local health department preparedness and response capabilities relative to Bioterrorism. The purpose of the initiative is to upgrade capacity quickly for a response to a terrorist attack with biologic or chemical agents. A concomitant effect of this major initiative will be the general improvement of the disease surveillance system, with broad benefit to the public.

The probability of a significant terrorist attack with a biologic agent in the United States is not known, but the consequences could be grave. This issue is a priority for public health, which has committed to the timely strengthening of its rapid response and disease investigation systems. The system is ready now to respond to terrorist events. In the coming months, public health resources will be improved at the local, city, state and federal levels.

What biological and chemical threats will be addressed? Although the system will provide a systematic response capability for numerous biologic and chemical agents, capacity will be developed quickly for a group of agents that are considered highest risk. The biologic agents (diseases) that are identified as a priority are *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), *Francisella tularemia* (tularemia), *Brucella* species (brucellosis), *Variola* (smallpox) and *Clostridium botulinum* toxin (botulism). The chemical agents are organophosphates, mustard gas and Ricin. A large number of chemical agents, in addition to the highest risk agents, will be detected by the analytical procedures that have been developed for screening. In addition to clinical specimens, environmental samples are anticipated as routine test requests for biologic agent protocols.

What is the strategy for achieving such a major reinforcement of our core public health system? A strategic planning effort, which was coordinated by CDC, brought together federal, state and local health experts, military scientists and the Federal Bureau of Investigation. Through this work, an implementation plan was developed to address five areas identified as key to emergency preparedness: 1) Preparedness Planning and Readiness Assessment, 2) Surveillance and Epidemiologic Capacity, 3) Laboratory Capacity for Biologic Agents, 4) Laboratory Capacity for Chemical Agents and 5) Health Alert Network and Training. The current RFA provides discrete funding initiatives for each of these components, and for their integration.

Preparedness Planning and Readiness Assessment will support the development of statewide plans that link and integrate health departments, emergency response teams and law enforcement agencies for improved response to terrorist threats. Initiatives are already underway in Massachusetts to link resources and communication for rapid and effective response to threat events.

Surveillance and Epidemiology Capacity initiatives will strengthen systems for rapid detection of unusual outbreaks of illness that may be the result of terrorism using biologic or chemical weapons.

Laboratory Capacity for Biologic Agents will assure that diagnostic capabilities for bioterrorist agents are available at all state and major city public health laboratories. The funding will enable these laboratories to conduct rapid diagnostic and reference testing for the priority biologic agents.

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Detection of a Bioterrorist Event - A clinical and public health laboratory partnership

Clinical and public health laboratories form a critical link in the early warning and rapid response system for emerging infectious diseases and disease outbreaks. The specimens submitted from clinical laboratories to public health laboratories are monitored to detect trends in prevalence of infections or identify a potential common source of exposure. As molecular diagnostic methods have advanced, the sensitivity and specificity of the laboratory-based monitoring system has increased. For example, a recent outbreak of *Listeriosis monocytogenes* was detected with laboratory data from a small number of cases, with a wide geographic distribution in the United States, when pulsed field gel electrophoresis patterns were matched. Laboratory-based surveillance can identify previously unrecognized associations of microbes with clinical disease, shifts in the genetic composition of microbes such as influenza, trends in antimicrobial resistance to antibiotics and the emergence of new

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Laboratory Capacity for Chemical Agents will develop rapid testing capacity at four regional state public health laboratories for diagnostic capabilities to screen clinical specimens for chemical agents.

Health Alert Network and Training will establish and maintain a communication network that will support the exchange of information over the Internet, rapidly disseminate public health advisories and provide training for health workers in core competencies.

Applications from health agencies are due at CDC by May 14, 1999. The Massachusetts Department of Public Health plans to respond to all components of the announcement. MDPH will be working with its partners in public health at the local level, and with emergency response agencies to assure that the application represents a coordinated proposal, which reflects the many critical components to an effective emergency response.

Inquiries and questions concerning the laboratory capacity components of the Bioterrorism initiatives should be addressed to Ralph Timperi, Assistant Commissioner, State Laboratory Institute (telephone 617-983-6201, Fax 617-983-6210, e-mail, ralph.timperi@state.ma.us).

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pathogens. This existing surveillance will be one means of detecting a Bioterrorist event.

SLI has provided reference diagnostic microbiologic testing for over 40 years. Each day, numerous clinical isolates that are not identified, or not completely characterized, by conventional automated and manual microbiologic procedures are sent to SLI from hospitals. Using a comprehensive testing algorithm, pathogens ranging from *Bacillus anthracis* to *Yersinia pestis* are identified at SLI and CDC.

In the coming months, the referral of clinical isolates to SLI will be emphasized to increase the specimen flow and sensitivity of this early warning system. The use of very rapid and highly specific tests will provide data to the public health network, which can detect the occurrence of an unusual increase in the incidence of a disease or infection with a pathogen not endemic in the geographic area of the patient. Test data will be reported by electronic means to the federal Centers for Disease Control and Prevention (CDC) and unexpected events will be investigated quickly by epidemiologists at the local, state and federal level. DNA fingerprinting technology will permit matching of clinical cases even when the numbers are small and the people affected may have dispersed widely following an exposure.

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Quality Assurance & Regulations

Laboratory Information Systems (LIS) Validation

by Dina Caloggero

Laboratory Information Systems (LIS) have become essential tools with constantly expanding roles in the diagnostic testing process. Their validity must be assessed just as laboratory instruments are evaluated. The validation process ensures that all components of the LIS, including the hardware, software and peripheral devices, function properly. Both the Food and Drug Administration (FDA) and the Health Care Financing Administration (HCFA) have regulations dealing with LIS validation. Voluntary accreditation agencies, such as the College of American Pathologists (CAP), also have guidelines requiring LIS validation.

LIS validation is performed at two levels. First, the provider of the system, whether it is written by in-house programmers or an outside vendor, is responsible for assuring that the system operates as described in its specifications. This documented information must be supplied to the user by the vendor or in-house programmer. Secondly, the individual laboratory utilizing the system must test the system using its own standard operating procedures, database elements, etc., and must document the results.

A successful laboratory LIS validation begins with a comprehensive plan. The plan should define and challenge the limits of the system, including data entry, storage and retrieval. Both abnormal and normal data must be used to test the system. Parallel testing can be used in part to accomplish this; however, it must be supplemented with grossly abnormal results that may not occur during the parallel testing period. In some cases it is more advantageous to use simulated results to test the limits of the system. Both screen displays and printed reports should be compared for accuracy, clarity and completeness. Personnel must also be trained and checked for competency prior to implementation of the LIS.

Documentation of the system validation must include the functions tested, how they were tested and by whom, and the results and conclusions. All documentation must be reviewed and approved by the laboratory director.

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Program Reports — Pertussis (Whooping Cough)

The classical definition of pertussis is an acute, highly communicable bacterial disease characterized by a paroxysmal or spasmodic cough. These symptoms usually end in a prolonged, high-pitched inspiration, known as the whoop. However, this characteristic whoop is not normally present in teenagers and adults, where the only symptoms may be prolonged coughing.

The causative agent of this disease is *Bordetella pertussis*, a small, nonmotile, gram-negative coccobacillus. Pertussis is highly contagious and transmitted by aspiration of this bacteria sprayed into the air by patient coughing. Infectivity usually wanes by the third week following onset of symptoms.

The United States, as well as other countries, is experiencing a dramatic increase in what was thought to be a childhood disease eliminated by universal immunization. What has not been appreciated until recently, is the fact that childhood immunization is not permanent. Immunity is usually lost by age10 to 12. Thus the presence of pertussis in one individual, e.g., an unvaccinated infant, a child who has not completed the vaccination series or a teenager / adult whose immunity has waned, can easily be transmitted to the susceptible populations. These disease outbreaks, frequently affecting entire school grades, are readily diagnosed by physicians in Massachusetts as a result of our unique pertussis testing algorithm. Early recognition of pertussis permits antibiotic prophylaxis to prevent the school based outbreaks from spreading throughout the community.

Unlike most other state laboratories, we provide two distinct forms of testing for pertussis, i.e., culture and single-specimen serology. The culture is recommended for all children under the age of 11. For all other individuals, culture is the test of choice during the first two weeks following onset, and serology after 2-weeks.

The State Laboratory provides culture collection kits, consisting of a swab, a casamino acid wetting solution and a Regan-Lowe (charcoal) transport slant containing cephalexin. When the inoculated specimens are received in our laboratory, the slants are swabbed to remove bacterial growth and streaked onto Bordet-Gengou (BG) medium containing methicillin. Both the transport medium and the BG plates are incubated at 35^{o} C for up to 7 days. Classical biochemical and immunologic techniques are used to identify the presence of *B. pertussis*.

Our laboratory offers a unique, in-house developed, single specimen serological test for the IgG antibody to pertussis toxin. This assay is an ELISA technique performed in a microtiter format. An antibody concentration of $\geq$ 20 μg / dL is interpreted as diagnostic for a current or recent infection with *B. pertussis*. Most other laboratories require acute and convalescent sera, looking for a 4-fold rise in titer; hence, the results from these assays are of greater epidemiological than diagnostic value.

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Each state has a public health laboratory (SPHL) that will have the capacity to screen specimens to rule out or presumptively identify the biologic agents of concern. Many SPHL, including SLI, have biosafety level 3 (BSL-3) facilities and advanced technology to enable manipulation of high-risk infectious agents and sub-species characterization. CDC will support this system with technology, reagents, and reference testing. In addition, CDC and the National Laboratory Training Network will develop distance learning programs and other training products to meet the needs of the surveillance and laboratory networks. Several SPHL will have regional and national responsibilities to provide sub-species typing and / or surge testing capacity for the national public health network.

As SPHL capacity is strengthened in the coming months to broaden response capacity for Bioterrorism, the effects of these infrastructure improvements will be seen in laboratory-based surveillance for naturally occurring diseases as well. Continual updating of test methods will provide more timely and accurate data with enhanced clinical relevance and epidemiologic value. The infrastructure improvements will include electronic data interchange, so that the detailed molecular data that is promptly generated from tests are available to public health and clinical practitioners, who will be able to more effectively manage outbreaks, prevent the spread of disease and treat patients.

SLI has a Bioterrorism Preparedness Team that is on-call 7 days-24 hours. This team supports first responders through the state emergency management system. Integrated with our current laboratory capacity, the response team expedites tests of clinical and environmental samples for biologic agents as events occur. The system is geared to rapidly evaluate hoaxes and real exposures to support management of emergency events.

Inquiries concerning the SLI Bioterrorism operations should be directed to Ralph Timperi, Director, State Laboratory Institute.

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for the electronic version of this newsletter and other information about the State Laboratory Institute: www.state.ma.us/dph/bls.

Laboratory Training Activities

Pulsed Field Gel Electrophoresis National Meeting - May 3-4, Swissotel, Boston, MA. Open to staff of state public health laboratories that are participants in the PulseNet program. Contact Heather Christiano at APHL HQ, (202) 822-5227 X202.

STD Prevention Training Center Courses, State Laboratory Institute, Boston, MA. Syphilis Serology, 1-day, May 13; STD Intensive, 3-day, April 26-28 and May 24-26; Stained Smears, April 28 AM; Wet Mounts, April 28 PM. Call (617) 983-6945.

Public Health Teleconference Series, State Laboratory Institute, Boston, MA. Hepatitis C, May 25; Vancomycin Resistance, June 22; Influenza, October 19; *Chlamydia trachomatis*, November 16. Fee $25 per site per program. Call (617) 983-6285.

State Laboratory Training Coordinator, *Garry R. Greer, BS, (617) 983-6608, E-mail: garry.greer@state.ma.us.*
For a list of NLTN courses in your area sign on to the Web at http://www.cdc.gov/phppo/dls/nltn.htm.

The State Laboratory Institute Newsletter is a free monthly publication of the Bureau of Laboratory Sciences

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